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What's new in spine surgery

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SPECIALTY UPDATE

What's New in Spine Surgery

By Keith H. Bridwell, MD, Paul A. Anderson, MD, Scott D. Boden, MD, Alexander R. Vaccaro, MD, and Jeffrey C. Wang, MD

What's New in the Treatment of the Cervical Spine***Cervical Disc Arthroplasty***

Three cervical disc arthroplasty devices are currently approved for patient care in the United States. There are different kinematic designs (ball and socket, ball and trough, and mobile center core) and different bearing couples (stainless steel metal on metal, cobalt-chromium on polyethylene, and titanium on polycarbonate-polyurethane). Other designs with cobalt-chromium metal-on-metal bearing surfaces are also being investigated in pivotal clinical trials. No clinical differences are apparent between these devices at this time. The four and five-year results of randomized clinical trials comparing arthrodesis with arthroplasty after decompression for the treatment of single-level cervical disease have shown equal or better results following arthroplasty as compared with arthrodesis in terms of overall clinical success, pain, and functional improvement, and the results have been stable over time. Revision rates of 2% to 5% have been seen following arthroplasty, and in these trials no device failures or wear-associated complications have been observed. Pooled data indicate that the rates of reoperation are significantly higher following arthrodesis, at both the index and adjacent levels. Two cases of apparent metal hypersensitivity causing a pseudotumor with symptomatic spinal cord compression following the placement of a cobalt-chromium metal-on-metal cervical prosthesis have been reported. These cases were similar to the pseudotumor reactions seen in some patients following metal-on-metal total hip arthroplasty.

Anterior Cervical Discectomy and Fusion

Anterior cervical discectomy and fusion remains the most common surgical procedure involving the cervical spine and

is associated with a high level of patient satisfaction. Comparative effectiveness and cost-effectiveness studies also have demonstrated the value of this procedure in comparison with the treatment of other orthopaedic and general medical diseases. A longitudinal National Inpatient Database study demonstrated that the total number of dollars spent for anterior cervical spine surgery increased sixfold from 1992 to 2005 despite the hospital stay decreasing by half. Surgical procedures for patients with more comorbidities are being increasingly performed. When the Short Form (SF)-36 was used to assess outcomes, improvement after cervical arthroplasty and arthrodesis was equal to that after total hip or total knee arthroplasty. Evaluating procedural costs is difficult and varies widely, but in one report at a single institution, up to a fivefold variation of costs occurred for single-level cervical fusions. The cost disparities were related to variation in the length of hospital stay and the surgeon's choice of medical equipment, including implant cost. Costs were inversely proportional to the volume of surgery as patients of high-volume surgeons had shorter length of stay and lower equipment costs. Given the limited clinical data supporting one device over another, surgeons should consider cost when selecting these implants.

The United States Food and Drug Administration (FDA) sent a warning letter in July 2008 regarding the use of recombinant human bone morphogenetic protein-2 (rhBMP-2) for anterior cervical spine surgery because there had been many reports of postoperative severe dysphagia, dysphonia, hematoma, and airway obstruction. These problems were confirmed in a randomized clinical trial in which rhBMP-2 was compared with ceramic bone filler, with both being placed into a cage along with an anterior cervical plate. The BMP-2 was associated with significantly greater dysphagia scores, requirement for steroids to reduce retropharyngeal swelling, and ectopic bone posterior to the cage toward the spinal cord and at adjacent levels, without any observable

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difference in fusion. Bioabsorbable plates have been used, but the results of a small observational cohort were disappointing, showing early failure, graft collapse and extrusion, pseudarthrosis, and segmental kyphosis in more than half of the patients.

Cervical Myelopathy

No consensus has been reached in determining the choice of either anterior or posterior approach for the surgical treatment of cervical myelopathy. The choice will depend on many factors such as the number of involved levels, the cause of compression, spinal alignment, comorbidities, and the surgeon's experience and ability. In a large international multicenter observational study, investigators found significant improvement in all outcome measures for patients managed with both anterior and posterior approaches.

The management of patients who have mild symptomatic myelopathy or those who have cervical stenosis without neurologic symptoms remains controversial. It is unknown if surgical decompression will lead to improved outcomes and will prevent deterioration or spinal cord injury with subsequent trauma. Sumi et al. reported on seventy patients with mild cervical spondylotic myelopathy who were managed nonoperatively for five years. Deterioration occurred in 25% of the patients, the majority of whom were subsequently managed surgically. In these cases, severe cord compression was present initially and magnetic resonance imaging demonstrated a triangular deformity of the spinal cord, a finding that may warrant earlier surgical decompression. The need for earlier surgical decompression was confirmed in a European study that examined the natural history of cervical myelopathy due to long surgical waiting lists. Patients with myelopathy had to wait more than twenty months for surgery; more than two-thirds of these patients had deterioration in terms of pain and function and half had deterioration as demonstrated by objective neurologic examination. Only one patient had improvement despite having no active treatment.

Another concern in patients with cervical cord compression is the chance of catastrophic spinal cord injury resulting from low-energy trauma. In a Japanese multicenter study, 453 patients with acute traumatic spinal cord injury were reviewed. Of these, 25% had ossification of the posterior longitudinal ligament and did not have associated bone injury. Half of the patients had clinical symptoms prior to acute spinal cord injury, such as gait disturbance, and only one-quarter of the patients were aware of the diagnosis of ossification of the posterior longitudinal ligament. The mechanism of spinal cord injury was a fall in >70% of the cases. Although this study did not answer the question of whether prophylactic decompression will reduce risk of spinal cord injury in patients with asymptomatic spinal cord compression, certainly patients with symptomatic myelopathy such as ataxia are at risk for spinal cord injury with subsequent trauma.

What's New in Biologic Topics Related to the Spine *Introduction*

Biologics continue to be a major focus in spinal research and the development of new products for patients with spinal disorders today. The majority of the clinical attention remains on bone formation, but laboratory efforts continue to investigate the role of biologics in retarding or reversing intervertebral disc degeneration. In patients undergoing spinal fusion, the choice of bone-graft substitutes remains an imperfect process, made difficult by the paucity of clinical data, a preponderance of anecdotal information and marketing, and the reality of price differences between materials. Regardless, the desire to eliminate the need for autogenous iliac crest bone graft harvest remains strong, and the use of biologics is on the rise. Since the FDA's post-marketing approval of recombinant human bone morphogenetic protein-2 (rhBMP-2) in 2002 and Humanitarian Device Exemption for rhBMP-7 late in 2004, the majority of new studies have continued to focus on the clinical performance and local side effects resulting from physician-directed use of rhBMP-2. A recent survey in the United States estimated that BMPs were used in 25% of spinal fusions in 2006.

Recombinant Osteoinductive Proteins

In the past year, there were no reports of new clinical studies on spinal fusion using rhBMP-7 (OP-1; Stryker, Hopkinton, Massachusetts). This biologic failed to achieve post-marketing approval for posterolateral spine fusion in 2009. A study of rat fracture repair demonstrated that OP-1 could mitigate the inhibitory effects of glucocorticoid exposure, suggesting that BMPs may be effective even in patients taking steroids. However, it is not clear if higher concentrations of BMPs will be required in such situations clinically.

Although rhBMP-2 (INFUSE; Medtronic Spinal & Biologics, Memphis, Tennessee) has received FDA approval for anterior lumbar interbody fusion, several physician-directed and Investigational Device Exemption studies have demonstrated outcomes of transforaminal and posterior interbody spine fusions as well as posterolateral spine fusion. A pilot study involving forty-six patients investigated the use of an rhBMP-2/collagen sponge with ceramic granules as a bulking agent inside the sponge for posterolateral lumbar spine fusion. This technique yielded a 95% radiographic fusion rate in the BMP group, compared with a 70% fusion rate when iliac crest bone graft was used alone. Another report involving 463 patients undergoing scoliosis surgery described the use of rhBMP-2 with an optimized compression-resistant matrix instead of a collagen sponge, resulting in a 96% fusion success rate as compared with an 89% rate for patients managed with iliac crest bone graft.

Another important application for BMPs is long spinal deformity fusion. The acquisition of adequate iliac crest bone graft in such cases is consistently a challenge. One report from a major spinal deformity surgical center described the

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successful use of rhBMP-2/collagen in these patients, with an average rhBMP-2 dose of 10.0 mg/level for posterior fusions and 11.6 mg/level for anterior fusions. This study demonstrated a pseudarthrosis rate of 28% in patients who received iliac crest bone graft and of only 4% in the patients who received rhBMP-2.

A primary concern with physician-directed use of recombinant BMPs continues to focus around local adverse events. The most commonly reported local side effects are heterotopic bone formation in the surgical approach track, transient radiculitis, transient vertebral body bone resorption when used near exposed cancellous bone, and sterile seroma fluid collections and/or local edema. Most of these local side effects are believed to be related to use of excessive BMP, either by increasing the concentration of the growth factor on the carrier sponge or overfilling the defect with the BMP sponge composite, resulting in a higher concentration or leakage of BMP into the surrounding tissues. BMP-induced radiculitis typically occurs seven to ten days following surgery and persists for a variable length of time.

Although no prospective studies have yet been reported, anecdotal publications have described two methods to potentially lower the risk of these local side effects, particularly with posterior lumbar interbody fusion and transforaminal lumbar interbody fusion procedures. One report on seventeen patients undergoing posterior lumbar interbody fusion with PEEK (polyetheretherketone) cages and 6 mg of rhBMP-2 per cage described no clinical side effects but described some transient radiographic resorption of the vertebral end plates. The general consensus is that lower doses of rhBMP-2/collagen when used in the interbody space may decrease the complication rate. A study supporting the dose-dependence of complications, presented at the North American Spine Society annual meeting but not yet published, involving a subgroup of patients who received a dose of <1.1 mg of rhBMP-2 per level for transforaminal lumbar interbody fusion or posterior lumbar interbody fusion combined with demineralized bone matrix, demonstrated a 95% fusion rate, with no complications.

There have been several reports of psoas muscle ossification associated with rhBMP-2/absorbable collagen sponge implantation in the posterolateral spine, but it is believed that this is uncommon. Nonetheless, there appears to be something unique about the psoas muscle, compared with other posterior spinal muscles, that may make it more susceptible to BMP-2-induced heterotopic ossification in some individuals. The risk factors that lead to this rare side effect are not known but may involve both genetic predisposition as well as surgical violation of the intertransverse membrane providing access to the psoas muscle.

Several authors have previously reported severe perioperative swelling in the anterior cervical spine, sometimes when excessive BMP-2 doses were used or when the BMP was placed outside the structural cage/implant. This complication

often becomes apparent several days after surgery and has necessitated reintubation or tracheotomy because of the risk of respiratory arrest. Surgeons who are experiencing these local side effects with any regularity should carefully examine their technique and should avoid the use of excessive amounts of BMPs in small spaces or overpacking of the BMP implants. Given the high success rate for anterior cervical fusion in healthy patients managed with allograft and plating, surgeons must carefully balance any increased risk of side effects resulting from the use of BMP in those patients with a higher risk of nonunion, such as those with diabetes, smokers, those receiving corticosteroid treatment, or those with multi-level cervical fusion. A recent survey of complications associated with spine fusions demonstrated that the use of BMP in anterior cervical fusion procedures increased the complication rate from 4.7% to 7.1% and was associated with greater inpatient hospital charges across all categories of spine fusion.

Other Bone Graft Substitutes

Although much focus remains on recombinant osteoinductive proteins, their relatively high cost has continued to encourage research involving other bone-graft solutions. Platelet-rich plasma was offered as an autologous growth factor source to augment bone healing, but it then fell out of favor for use in spine fusion when several clinical studies demonstrated relatively poor results. A recent study of mouse spine fusions showed that bone marrow cells were able to augment the effects of rhBMP-2 but that platelet-rich plasma was unable to do so. In contrast, a new study demonstrated that platelet-rich plasma increased the osteoinductivity of demineralized bone matrix *in vivo*, but only when the platelet-rich plasma was used without thrombin activation. This information may prompt a reevaluation of platelet-rich plasma for augmentation of bone healing, ideally in carefully controlled preclinical studies.

There is continued interest in the use of mesenchymal stem cells for bone and cartilage regeneration. In rodent models, both fat-derived and bone marrow-derived mesenchymal stem cells have been proposed for use in spine fusion. However, spine fusion is a challenging environment in which to form bone, and a recent study showed that neither bone marrow aspirate nor mesenchymal stem cell-enriched bone marrow aspirate was sufficient to heal critical-size femoral defects in rats. Furthermore, another study demonstrated that BMP was not able to induce an osteogenic response in adipose-derived mesenchymal stem cells, suggesting that not all sources of mesenchymal stem cells may be sufficient for spine fusion. The clinical future of these strategies that propose the use of mesenchymal stem cells alone as a biologic grafting solution for spine fusion remains unclear. The number of stem cells present in bone marrow is relatively small and variable, and in the absence of specific signals (e.g., BMP) it is not clear whether sufficient numbers of cells are present to consistently initiate bone formation in spine fusion.

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Biologic Treatments for Disc Degeneration

Progress toward biologic treatments to prevent or retard disc degeneration or to heal anular defects continued at a slow pace. Continued animal evidence of beneficial effects of recombinant BMPs (BMP-7, BMP-2, GDF-5) on disc metabolism have prompted the planning of a clinical trial to investigate the response in humans, but no results have been published to date. Indicating that BMPs may have beneficial effects on discs, an in vitro study demonstrated different effects of BMP-2 on human anulus fibrosus and nucleus pulposus cells. There was a mitogenic effect on anulus fibrosus cells and an anabolic stimulation of proteoglycan synthesis in the nucleus pulposus cells, with no evidence of bone formation within the disc tissue. Although the use of biologics to treat disc degeneration is a long way off from clinical use, it is worth monitoring developments in this area that could ultimately be applicable for the treatment and prevention of many degenerative spine disorders.

What's New in Spinal Deformity Surgery

Idiopathic Scoliosis

There is continued interest in the comparison between anterior and posterior treatment of thoracolumbar and lumbar adolescent idiopathic scoliosis. Reports comparing the two methods and analyzing either posterior-only or anterior-only approaches have indicated that both techniques have merit.

The value of pedicle screws continues to be a point of investigation. In the idiopathic teenage population, it appears that maneuvers with pedicle screw constructs provide more deformity correction and derotation than do hybrid constructs, hooks-only constructs, or wires-only constructs. It also appears that derotation maneuvers with pedicle screws provide better correction than what is seen with hooks. However, it is unclear whether derotation maneuvers with pedicle screws provide better three-dimensional correction than other maneuvers with pedicle screws do. It may be that the enhanced correction with pedicle screws is due to the coupled effect of translational to rotational correction.

Bracing for Idiopathic Scoliosis

There continues to be substantial debate about the usefulness of bracing. One study in which patients who were managed with bracing were compared with patients who were managed with observation resulted in interesting conclusions at the time of long-term follow-up. The patients in the observation group found their body appearance to be significantly less distorted than did those in the bracing group. Also, there is some suggestion that patients who are managed with bracing before posterior fusion and instrumentation for the treatment of idiopathic scoliosis have reduced satisfaction, lower activity levels, and more pain two years after surgery than those who are not managed with bracing preoperatively. Furthermore, decision-making about who should be managed with bracing on the basis of genetic factors is being studied and adds an additional component.

Adult Spinal Deformity

Spinal deformity in adults presents differently on the basis of age. Patients who are more than sixty years old have significantly greater disability and worse health status in comparison with those who are forty to sixty years old. While patients who are more than sixty years old have more operative complications, their incremental improvement in terms of patient-reported health status following surgical treatment seems comparable with or slightly higher than that of younger patients at the time of the two-year follow-up as determined with outcome-assessment questionnaires. Appropriately selected patients over the age of sixty years do appear to benefit from long fusion to the sacrum for the primary treatment of adult scoliosis. Several emerging studies suggest that nonoperative treatment, commonly used for patients with adult scoliosis, results in substantial cost but no improvement in health status. The NIH R01 study entitled "A Multicenter Prospective Study of Quality of Life in Adult Scoliosis (ASLS)" (NCT00854828) is about to begin enrollment.

Biologics

In the past, iliac bone graft has been used for fusion with posterior instrumentation for the treatment of adolescent idiopathic scoliosis. Most surgeons and centers are now trending away from the use of iliac bone graft, using local bone and allograft instead. One report suggested a high fusion rate (>95%) in association with the use of local bone and beta-tricalcium phosphate matrix, without the need for allograft.

Several studies in adults have suggested that, in long spinal fusions with instrumentation to the pelvis and sacrum, iliac crest bone graft may not be necessary if rhBMP-2 is combined with local autograft and allograft. Fusion rates associated with rhBMP-2 were better than those associated with iliac bone graft without rhBMP-2 for multilevel fusions performed from either an anterior or a posterior surgical approach (96% compared with 72% in one study). However, nonunion is relatively common, particularly at L5-S1, even with anterior lumbar interbody fusion, transforaminal lumbar interbody fusion, and protection of sacral screws with iliac screws. Outcomes associated with transforaminal lumbar interbody fusion and/or anterior lumbar interbody fusion at L5-S1 seem to be comparable. Most centers are now performing more selective anterior fusions of two or three segments. In addition, utilization of minimally invasive multilevel anterior fusion techniques is increasing. Clinical and radiographic comparisons of open and minimally invasive techniques will soon be available.

Infantile and Juvenile Scoliosis

Various techniques are currently being employed to treat progressive spinal deformity in the infantile and juvenile age ranges (zero to ten years old). In this population of patients with early-onset scoliosis, a long fusion negatively impacts ultimate trunk height and pulmonary maturation. The issues noted in association with various "growing rod" techniques are

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(1) the high prevalence of growing rod fractures, (2) the role of neuromonitoring for growing rod and rib-based instrumentation surgery, (3) the high prevalence of infection and implant-related pressure sores, (4) the identification of spontaneous autofusions, (5) diminishing return with subsequent lengthening procedures, (6) the ultimate benefit in terms of pulmonary function, and (7) the true prevalence of neural axis anomalies in these patients. Currently, all of these issues are being studied.

Spondylolisthesis

One study reviewed forty-three patients who underwent surgery for the treatment of spondylolisthesis or spondylolysis between 1984 and 2005 at two institutions and demonstrated an overall complication rate of 47% after a minimum two-year follow-up. In this series, a postoperative neurologic deficit was seen in 12%, 80% of which persisted at the time of the final follow-up. In the group as a whole, 37% required reoperation and 5% had wound infections. In children and adolescents, the complication and reoperation rates following surgery for the treatment of spondylolisthesis are much higher than those following surgery for the treatment of idiopathic scoliosis.

Osteotomies

Several studies have compared one-column posterior osteotomies with three-column posterior osteotomies for the correction of spinal deformity. While greater correction is achieved with three-column osteotomies, this technique is associated with greater blood loss, greater neurologic risk, and higher overall complication rates. The role of either posterior one-column or three-column osteotomies is gaining importance for the treatment of sagittal imbalance. Determination of the appropriate cephalad instrumented vertebra in adult spinal deformity remains a challenge. Controversy remains with regard to what factors impact the outcome of fusions that extend to the upper or lower thoracic spine, but long-term evaluations now clearly favor extension of the fusion to the sacrum instead of L5 in the adult population.

Patient-Reported Outcomes

Previous studies suggested the SRS-22 outcomes tool was not responsive to the effects of surgical treatment of adolescent idiopathic scoliosis, but several reports at the 2009 Scoliosis Research Society (SRS) annual meeting suggested the contrary. A substantial percentage of patients with adolescent idiopathic scoliosis reported reduction in pain, improved appearance, and high satisfaction with surgical treatment. For the adult population, the SRS, Oswestry Disability Index (ODI), and SF-12 outcomes tools seemed to reflect improvement following surgical treatment. On the SF-12, improvement in the physical component was consistent but improvement in the mental component proved to be inconsistent. Of the three measures, the SRS-22 seems to be the most sensitive to change as a result of surgical treatment.

Complications

The rate of postoperative blindness complicating long spinal surgery with the patient in the prone position is 1 in 1000 (0.1%). This devastating complication is as feared as paralysis. Visual-evoked potentials have been suggested as a potential monitoring tool. Recommendations include keeping all pressure off the eyes, having the head and face higher than the rest of the body, and avoiding long periods of hypotension if the surgery lasts for more than six hours.

The SRS Morbidity and Mortality Committee analyzed postoperative infection: 108,419 cases were identified, with a 0.8% rate of superficial infection and a 1.3% rate of deep infection. The conclusion of the Morbidity and Mortality Committee was that "post-surgical infection, even among skilled spine surgeons, is an inherent potential complication." Among the adult population, the highest deep infection rates were found in patients with kyphotic and degenerative scoliosis. In the pediatric population, neuromuscular kyphosis was associated with the highest rate of deep infection, approaching 10%.

What's New in Spinal Cord Injury

Injuries involving the spinal cord continue to be devastating. Recent research efforts have focused on the timing of surgical intervention and the use of newly developed pharmaceutical agents to minimize injury or to promote nerve regeneration, with several of these drugs involved in human trials. The use of methylprednisolone continues to be controversial, with emerging evidence arguing against its use.

Evaluation and Management

Proper evaluation of traumatic spinal cord injuries and care at an appropriate facility is essential. In a recent review of approximately 11,000 patients that was published in the *Annals of Surgery*, patients with a traumatic spinal cord injury who were managed at either a level-I or II trauma center were less likely to have paralysis at the time of discharge (odds ratio, 0.67). Interestingly, higher surgical volume, and not admission volume, was associated with a lower risk of paralysis. Admission to a trauma center or a non-trauma center did not affect mortality. Despite recommendations that patients with traumatic spinal cord injuries be managed at a trauma center, approximately 42% of patients were cared for at a non-trauma center.

Early decompression has long been believed to be beneficial for the treatment of spinal cord injury, although clinical evidence to support this belief has been lacking. The Surgical Treatment for Acute Spinal Cord Injury Study (STASCIS), a multicenter, randomized clinical trial, is addressing this issue. In that study, early surgery is defined as that performed within twenty-four hours after the injury whereas late surgery is defined as that performed more than twenty-four hours after the injury. As of August 2009, >400 patients had been enrolled. While the patients who were managed with both early and late surgery showed improvement of one American Spinal

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Injury Association grade, a higher percentage of the patients who were managed with early decompression showed improvement of two grades or more and those who were managed with late decompression were more likely to show no improvement or to have a deterioration in neurologic status.

Complication Avoidance

The development of heterotopic ossification, particularly around the hips, can be a challenging complication following spinal cord injury. In a recent study from Serbia, patients were randomized to have no preventive treatment or to receive pulsed low-intensity electromagnetic field therapy thirty minutes a day, for four weeks, starting seven weeks after the injury. No patient in the experimental group developed heterotopic ossification, but 33% of those in the control group did. It is theorized that the electromagnetic field treatment may increase blood flow to the areas of injury, increasing oxygen delivery and toxin removal, which may aid in the prevention of heterotopic ossification.

Neuroprotective Treatment

The use of methylprednisolone for the treatment of acute spinal cord injury continues to be controversial. Evidence supporting its use is derived from the National Acute Spinal Cord Injury Studies (NASCIS) II and III, although there has been considerable criticism of the methods used to demonstrate clinical usefulness. The lack of other effective treatment options, the high propensity for litigation in cases involving spinal cord injury, and the paucity of good clinical research opposing its use has led to methylprednisolone being widely used in the setting of spinal cord injury, including by 86% of members of the North American Spine Society. Recently, Ito et al. reported the results of a prospective cohort study from Japan in which patients who were managed during the first two years of the study received steroids, whereas patients who were managed during the second two years did not. The authors reported improved neurologic recovery in the group that did not receive steroids. They also reported a higher rate of complications in the group that received steroids, including higher rates of pneumonia and gastrointestinal bleeding. This study provides strong evidence to those who oppose the use of steroids for patients with spinal cord injury.

Emerging Therapies

The search for an effective treatment to help to improve neurologic function in patients with spinal cord injury is ongoing. Several pharmaceutical agents, medical devices, and interventions are currently undergoing clinical trials. Riluzole (sanofi-aventis, Bridgewater, New Jersey), a sodium channel-blocking medication currently approved for the treatment of amyotrophic lateral sclerosis, has been shown in animal studies to have neuroprotective properties at the zone of injury and is currently entered into a Phase-I clinical trial.

Magnesium chloride has previously been shown to have a beneficial effect in patients with spinal cord injury, but the high

doses necessary to produce a benefit have historically limited its usefulness. A new formulation incorporating the magnesium in polyethylene glycol, with the goal of increasing its bioavailability within the cerebrospinal space, has been developed. A Phase-I trial was recently completed, and plans are under way for a Phase-II trial. Cethrin (Alseres Pharmaceuticals, Hopkinton, Massachusetts) is a Rho GTPase inhibitor that acts to prevent apoptosis and to promote neurite growth. It has the ability to penetrate the spinal cord after extradural delivery. Currently, a combined Phase-I/IIa trial was completed, with no adverse effects being attributed to Cethrin. ATI355A2102 (Novartis, Basel, Switzerland) is an anti-Nogo A antibody that has been shown to promote neurite overgrowth and to promote axonal regeneration and functional improvement in a monkey model. An initial human trial is currently under way, and, while the initial results have shown no adverse effects, the final results from all arms of the study have yet to be evaluated. GRNOPC1 (Geron, Menlo Park, California), an allogeneic stem-cell-based therapy injected directly into the zone of injury within seven to fourteen days after the injury, has demonstrated improved neurite overgrowth, myelination, and motor function in animal models. A Phase-I clinical trial had been started, but as of August 18, 2009, the FDA has placed a hold on this study because of concerns regarding the formation of cysts in the post-injury scar. Although these cysts are nonproliferative and have been confined to the zone of injury, the FDA has requested additional animal studies before continuing with clinical trials.

The draining of cerebrospinal fluid and monitoring of intrathecal pressure has become routine following the treatment of aortic aneurysms but has not previously been evaluated in the setting of spinal cord injury. In a recent prospective randomized trial, Kwon et al. evaluated the effect of placement of a lumbar intrathecal drain and the drainage of cerebrospinal fluid to lower the intrathecal pressure in the setting of spinal cord injury. The authors suggested that the higher peak intrathecal pressures observed postoperatively in the group of patients who did not receive drainage of cerebrospinal fluid may have an adverse impact on the perfusion pressure of the spinal cord. In addition, the authors observed that the cerebrospinal fluid waveform was dampened initially and then increased in amplitude following decompressive surgery, suggesting the return of more normal cerebrospinal fluid flow across the zone of injury, and noted that this could be used intraoperatively to evaluate whether the decompression that has been performed is adequate. No change in neurologic recovery was found, but the small number of patients may have been inadequate to detect such a change. The authors suggested that the placement of an intrathecal drain may provide better monitoring of the perfusion pressure of the spinal cord following injury.

What's New in the Treatment of the Lumbar Spine

Lumbar spine disorders continue to be a substantial problem for the general population, and the cause and treatment of the

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pain generator for lumbar degenerative disease remains controversial.

Lumbar Disc Degeneration

Lumbar discography is a procedure that is commonly performed in an attempt to localize the pain generator and to determine whether the disc is the cause of the patient's low back pain. A prospective, controlled, matched-cohort study of disc degeneration, in which patients either had discography or did not, was performed. Seventy-five subjects without serious low back pain underwent a magnetic resonance imaging and discography protocol and were followed over a ten-year period. A matched group was also enrolled. Fifty patients undergoing discography and fifty-two control subjects were entered into the analysis. There was progression of disc degeneration in 35% of the patients in the discography group, compared with 14% of the subjects in the control group. There were fifty-five new disc herniations in the discography group, compared with twenty-two in the control group. These new disc herniations were disproportionately found on the side of the anular needle puncture. There were also more vertebral end plate signal changes and anular fissures, as well as greater loss of disc height and signal intensity, in the discography group. These findings are of concern because of the potential for the discography procedure to accelerate future disc degeneration.

Another study evaluated the surgery rate in patients having discography procedures. Two hundred and one consecutive patients with disc degeneration underwent discography to aid in localization of a possible source of back pain. On the basis of the results of the discography, 36% of the patients had recommendations against surgery, primarily based on a nonconcordant pain profile and three or more levels of concordant pain during the procedure. The authors concluded that discography can be a useful tool to identify patients who are not good candidates for surgery.

The cause of disc degeneration is not known but is thought to be multifactorial. One study specifically evaluated the effects of greater body mass on lumbar disc degeneration. Forty-four pairs of healthy male monozygotic twins with ≥ 8 kg of discordance in body weight were entered into the study. The authors found that higher body weight was associated with 6.2% higher bone density in the spine. They also found that there were fewer disc signal irregularities in the heavier twin as compared with the lighter twin, concluding that cumulative or repetitive loading due to higher body mass may slightly delay disc desiccation.

Vertebral Compression Fractures

A European multicenter randomized controlled clinical study was performed on patients with one to three nontraumatic vertebral compression fractures due to osteoporosis or cancer. Patients were assigned to either balloon kyphoplasty or nonoperative management. Twenty-one sites in eight countries enrolled 300 patients. Patients assigned to kyphoplasty had improved physical component scores, improved global quality

of life, more pain relief, less back disability, fewer days of limited activity, and less back pain. The authors concluded that balloon kyphoplasty improved the quality of life and reduced back pain and disability, without increasing adverse events, including the risk of vertebral fracture, over a two-year period.

Another study examined the risks of pulmonary cement embolism after multilevel vertebroplasty. In that study, 148 patients who had been managed with multilevel vertebroplasty had postoperative chest radiographs to assess for cement embolism. After a minimum duration of follow-up of two years, pulmonary cement embolism was confirmed in eleven patients, five of whom had pulmonary symptoms. All embolisms occurred in patients who had treatment of four levels or more, and none were found in patients who had procedures on different days.

Lumbar Disc Herniation

The length of time that patients with lumbar disc herniations experience symptoms before treatment and the results of the treatment are not known. The Spine Patient Outcomes Research Trial (SPORT) examined the correlation between the duration of symptoms and the results of treatment. The study involved 927 patients who had had symptoms for six months or less and 265 patients who had had symptoms for more than six months. The patients were analyzed as they were managed and followed for four years. At baseline, patients who had had symptoms for more than six months were likely to feel depressed, were less likely to believe that their symptoms were getting better, and were more likely to prefer surgical treatment. At the time of follow-up, all primary outcomes were significantly worse in patients who had had symptoms for more than six months. In the operative treatment group, patient satisfaction and the self-rated health trend were significantly higher among patients who had had symptoms for less than six months. In the nonoperative treatment group, these outcomes did not differ between the patients with symptoms for more than six months and those with symptoms for less than six months. In both the operative and nonoperative treatment groups, work status was significantly better in patients who had had symptoms for six months or less. Within both groups, the treatment effects were significant for all primary and secondary outcome measures at all follow-up time periods in favor of surgery. The authors concluded that increased symptom duration due to lumbar disc herniations is related to worse outcomes following both operative and nonoperative treatment.

A genetic predisposition for the development of lumbar disc disease has been suggested by several previous twin studies and genetic markers. In one study, 1294 patients with lumbar disc herniations were identified in a Utah population database. A comparison of the relatives of these individuals with those of >5000 patients without any lumbar disc herniations revealed a significant increase in the risk of disc disease in relatives. The risk of herniation was significantly elevated in both first and third-degree relatives. The findings of this study strongly support a heritable predisposition to lumbar disc herniation.

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Preoperative Studies

The relationship between preoperative electromyography studies and surgical results is not well documented. One study evaluated fifty-five patients who were evaluated with electromyography before undergoing surgical decompression with or without fusion. The preoperative electromyography studies were classified as positive or negative, and the patients were followed with regard to postoperative symptoms. The authors found that patients with primary extremity pain and a positive electromyography study had 78.1% improvement at the time of follow-up. Patients with extremity pain with a negative electromyography study had only a 20% improvement in terms of extremity pain. In patients who had primarily axial pain, the results of electromyography did not correlate with improvement in the back pain.

Evidence-Based Orthopaedics

The editorial staff of *The Journal* reviewed a large number of recently published research studies related to the musculoskeletal system that received a Level of Evidence grade of I. Over 100 medical journals were reviewed to identify these articles, all of which have high-quality study design. In addition to articles published previously in this journal or already cited in this update, twenty-one additional level-I articles were identified that were relevant to spine surgery. A list of those articles is appended to this review following the standard bibliography. We have provided a brief commentary about each of the articles to help guide your further reading, in an evidence-based fashion, in this subspecialty area.

Upcoming Meetings and Events Related to Spine Surgery

The EuroSpine Annual Meeting will be held on September 15 through 17, 2010, in Vienna, Austria. Web site: www.eurospine.org

The Forty-fifth Annual Meeting of the Scoliosis Research Society (SRS) will be held on September 21 through 24, 2010, in Kyoto, Japan. It will be preceded by a one-day course entitled "Cervical Spine Section," to be held on September 21, 2010. Web site: www.srs.org

The Twenty-fifth Annual Meeting of the North American Spine Society (NASS) will be held on October 5 through 9, 2010, in Orlando, Florida. There will be a number of precourses, to be held on October 4, 2010. Web site: www.spine.org

The Thirty-eighth Annual Meeting of the Cervical Spine Research Society (CSRS) will be held on December 2 through 4, 2010, in Charlotte, North Carolina. Web site: www.csrs.org

The Federation of Spine Associations will present the spine program on Specialty Day at the Annual Meeting of the American Academy of Orthopaedic Surgeons (AAOS) on February 19, 2011, in San Diego, California. Web site: www.aaos.org

The Annual Meeting of the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Section on Disorders of the Spine and Peripheral

Nerves will be held on March 9 through 12, 2011, in Phoenix, Arizona. Web site: www.spinesection.org

The Spine Arthroplasty Society's Eleventh Annual Global Symposium on Motion Preservation Technology will be held on April 26 through 29, 2011, in Las Vegas, Nevada. Web site: www.spinearthroplasty.org

The American Spinal Injury Association's (ASIA) International Conference on Spinal Cord Medicine and Rehabilitation will be held on June 4 through 8, 2011, in Washington, DC. Web site: www.asia-spinalinjury.org

The Annual Meeting of the International Society for the Study of the Lumbar Spine (ISSLS) will be held on June 14 through 18, 2011, in Gothenburg, Sweden. Web site: www.issls.org

The Eighteenth Annual International Meeting on Advanced Spine Techniques (IMAST) will be held on July 13 through 16, 2011, in Copenhagen, Denmark. Web site: www.imastonline.com

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Evidence-Based Articles Related to Spine Surgery

Andersen T, Christensen FB, Ernst C, Fruensgaard S, Østergaard J, Andersen JL, Rasmussen S, Niedermann B, Høy K, Helmig P, Holm R, Lindblad BE, Hansen ES, Egund N, Bünger C. The effect of electrical stimulation on lumbar spinal fusion in older patients: a randomized, controlled, multi-center trial: part 1: functional outcome. *Spine (Phila Pa 1976)*. 2009;34:2241-7.

This multicenter randomized controlled study demonstrated significantly better two-year improvement in three of four domains of the Dallas pain questionnaire in patients who had posterolateral fusion without instrumentation and who were managed with direct current stimulation. No differences were observed in terms of walking distance or SF-36 results.

Andersen T, Christensen FB, Egund N, Ernst C, Fruensgaard S, Østergaard J, Andersen JL, Rasmussen S, Niedermann B, Høy K, Helmig P, Holm R, Lindblad BE, Hansen ES, Bünger C. The effect of electrical stimulation on lumbar spinal fusion in older patients: a randomized, controlled, multi-center trial: part 2: fusion rates. *Spine (Phila Pa 1976)*. 2009;34:2248-53.

In a second study evaluating the radiographic results of a multicenter randomized trial, a low overall fusion rate occurred both in the group treated with electrical stimulation and in the group treated without stimulation, with no difference between the groups. Both this study and the previously mentioned study by Andersen et al. showed only a modest effect on outcome and demonstrated no radiographic improvement as a result of the electrical stimulation. The weaknesses of these studies included the variety of diagnoses and the potentially poor indications for fusion. Overall, these two studies failed to demonstrate any positive effect of direct current stimulation for in situ posterolateral lumbar spinal fusion.

Arts MP, Brand R, van den Akker ME, Koes BW, Bartels RH, Peul WC; Leiden-The Hague Spine Intervention Prognostic Study Group (SIPS). Tubular discectomy vs conventional microdiscectomy for sciatica: a randomized controlled trial. *JAMA*. 2009;302:149-58.

In this prospective, randomized trial, 167 patients who had undergone tubular discectomy were compared with 161 patients who had undergone conventional discectomy. Patients were followed for one year and were assessed with use of the Roland-Morris Disability Questionnaire, visual analog pain

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scores, and patient self-assessed recovery. There was no significant difference between the two methods in terms of Roland-Morris disability scores, but patients managed with tubular discectomy reported significantly worse leg and back visual-analog pain scores and self-assessed recovery scores. This well-done, level-I study disputes the findings of previous studies suggesting the superiority of minimally invasive surgery procedures and supports the continued use of conventional microdiscectomy.

Bakker EW, Verhagen AP, van Trijffel E, Lucas C, Koes BW. Spinal mechanical load as a risk factor for low back pain: a systematic review of prospective cohort studies. *Spine (Phila Pa 1976)*. 2009;34:E281-93.

This systematic review of the literature specifically assessed the effect of spinal mechanical load as a risk factor for low back pain. The authors evaluated the spinal mechanical load at work and during leisure activities in adults who were free of low back pain at the time of the baseline evaluation. They evaluated eighteen studies with a total of 24,315 subjects and found strong evidence that leisure-time sporting activities or exercises, sitting, and prolonged standing or walking are not associated with low back pain. There was conflicting evidence regarding the association between low back pain and leisure activities, whole-body vibration, nursing tasks, heavy physical work, and working with the trunk in a bent and/or twisted position. There was no evidence of an association between low back pain and sleeping or professional sporting activities. This excellent article disproves the theory that higher mechanical loads increase low back pain.

Buchbinder R, Osborne RH, Ebeling PR, Wark JD, Mitchell P, Wriedit C, Graves S, Staples MP, Murphy B. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med*. 2009;361:557-68.

Vertebroplasty has become a common treatment for painful osteoporotic vertebral fractures despite limited evidence to support its use. Seventy-eight patients with one or two painful fractures of less than twelve months' duration were enrolled in a prospective, randomized, double-blind, placebo-controlled trial. The authors were not able to find any significant advantage of vertebroplasty as compared with a sham procedure in patients with painful osteoporotic fractures. Sixty-eight percent of the patients in this study had fractures that were more than six weeks old; many surgeons would not consider vertebroplasty to be appropriate for such patients. There was a trend toward better outcomes in the vertebroplasty group, so it is possible that the study was underpowered to assess the benefit of vertebroplasty in patients with non-chronic vertebral fractures.

Carreon LY, Glassman SD, Djurasovic M, Campbell MJ, Puno RM, Johnson JR, Dimar JR 2nd. rhBMP-2 versus iliac crest bone graft for lumbar spine fusion in patients over 60 years of age: a cost-utility study. *Spine (Phila Pa 1976)*. 2009;34:238-43.

In this randomized clinical trial, patients who were more than sixty years of age who required decompression and posterolateral fusion were randomized to treatment with either rhBMP-2 or iliac crest bone graft. Patients who received iliac crest bone graft had more complications and an increased need for additional treatment and revision surgery in comparison with those who received rhBMP-2. Higher costs and lower improvement were seen in the group of patients who received iliac crest bone graft as compared with those who received rhBMP-2. This excellent article supports the benefits of rhBMP-2 over iliac crest bone graft for posterior lumbar fusion.

Cherkin DC, Sherman KJ, Avins AL, Erro JH, Ichikawa L, Barlow WE, Delaney K, Hawkes R, Hamilton L, Pressman A, Khalsa PS, Deyo RA. A randomized trial comparing acupuncture, simulated acupuncture, and usual care for chronic low back pain. *Arch Intern Med*. 2009;169:858-66.

This randomized trial compared acupuncture treatments in 638 patients with chronic low back pain. Ten treatments were provided over seven weeks and consisted of either individualized acupuncture, standardized acupuncture, simulated acupuncture, or usual care. All of the acupuncture treatments were associated with significant improvements on mean dysfunction

scales, and patients who had been managed with acupuncture were more likely to experience clinically meaningful improvements in terms of dysfunction, but not in terms of symptoms, as compared with the usual-care group at one year. Although acupuncture appeared to show some efficacy, the mechanism of action is unclear, especially when the simulated acupuncture group may represent a placebo effect. This excellent article evaluates some of the non-traditional treatments for low back pain and may affect the use of these modalities.

Chou R, Atlas SJ, Stanos SP, Rosenquist RW. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society Clinical Practice Guideline. *Spine (Phila Pa 1976)*. 2009;34:1078-93.

This systematic review of the literature, conducted through July 2008, assessed the benefits of nonsurgical interventional therapies for low back pain and radicular pain. The authors found that for sciatica or a prolapsed lumbar disc with radiculopathy, there was good evidence that chemonucleolysis is moderately superior to placebo injections but is inferior to surgery. Epidural steroid injections were moderately effective for short-term but not long-term relief. There was fair evidence that spinal cord stimulation was moderately effective for failed back surgery syndrome with persistent radiculopathy, although device-related complications were common. There was good or fair evidence that prolotherapy, facet joint injection, intradiscal steroid injections, and percutaneous intradiscal radiofrequency thermocoagulation are not effective. There was insufficient evidence to reliably evaluate other interventional therapies. This outstanding article examines the lack of data for many of the therapeutic strategies for low back pain.

Chou R, Baisden J, Carragee EJ, Resnick DK, Shaffer WO, Loeser JD. Surgery for low back pain: a review of the evidence for an American Pain Society Clinical Practice Guideline. *Spine (Phila Pa 1976)*. 2009;34:1094-109.

This systematic review of the literature, conducted through July 2008, examined the surgical treatments for low back pain. After an extensive search of the literature, the authors found that surgery for herniated discs associated with radiculopathy or symptomatic spinal stenosis demonstrates short-term benefits in comparison with nonoperative treatments, although these benefits can diminish with time. For low back pain with degenerative changes without radiculopathy, fusion is no more effective than intensive rehabilitation but is associated with moderate benefits in comparison with standard nonoperative therapy. This study represents an excellent literature-based review of the treatments for low back pain.

Dai LY, Jiang LS, Jiang SD. Posterior short-segment fixation with or without fusion for thoracolumbar burst fractures. A five to seven-year prospective randomized study. *J Bone Joint Surg Am*. 2009;91:1033-41.

The authors compared short-segment pedicular fixation with or without posterolateral fusion for the treatment of thoracolumbar stable-type burst fractures (fractures with no posterior ligamentous injury). Results at five to seven years showed no differences between groups. Implant-related complications were not different between the groups, and, surprisingly, implant removal was not required in patients without fusion. This study suggests that fixation without fusion is an option for patients with stable-type injuries; however, whether this generalizes to patients with greater heights and body mass indices as are seen in North America is unknown.

Han X, Zhu Y, Cui C, Wu Y. A meta-analysis of circumferential fusion versus instrumented posterolateral fusion in the lumbar spine. *Spine (Phila Pa 1976)*. 2009;34:E618-25.

The meta-analysis included four randomized controlled trials involving 437 patients with a primary diagnosis of low back pain with or without leg pain. The meta-analysis demonstrated that both procedures resulted in significant clinical benefit, although no difference was observed between the two techniques. Complication rates and fusion success rates were higher in the patients managed with circumferential fusion, whereas reoperation rates were lower.

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The weaknesses of this study include the low number of studies and patients, variations in surgical indications, and inconsistent surgical techniques, which limit the generalization of any conclusions.

Kallmes DF, Comstock BA, Heagerty PJ, Turner JA, Wilson DJ, Diamond TH, Edwards R, Gray LA, Stout L, Owen S, Hollingworth W, Ghdoke B, Annesley-Williams DJ, Ralston SH, Jarvik JG. A randomized trial of vertebroplasty for osteoporotic spinal fractures. *N Engl J Med.* 2009;361:569-79.

In this multicenter, prospective randomized trial, 131 patients with one to three painful vertebral compression fractures were managed with either vertebroplasty or a simulated procedure without cement (control group). The study did not show a significant improvement with regard to pain in the vertebroplasty group but did show a trend toward a meaningful improvement in terms of pain in the vertebroplasty group and a higher treatment crossover rate at three months in the control group. Perhaps the study lacked sufficient power to demonstrate these differences between groups. It is also worth noting that the authors had to lower the entry criteria to accept a pain level of 3 of 10, which many clinicians would not consider to be high enough to warrant a procedural intervention. The authors should be praised for their attempt to attain level-I evidence, but care must be taken before extrapolating this conclusion to the subset of patients with substantial levels of persistent pain at two to four weeks after acute vertebral fracture. That was not really the group of patients included in this study.

Koc Z, Ozcakar S, Sivrioglu K, Gurbet A, Kucukoglu S. Effectiveness of physical therapy and epidural steroid injections in lumbar spinal stenosis. *Spine (Phila Pa 1976).* 2009;34:985-9.

This randomized, single-blind controlled trial compared the effects of epidural steroid injections and physical therapy on pain and function in patients with lumbar spinal stenosis. Twenty-nine patients were randomized into three groups. Group 1 had inpatient physical therapy for two weeks, Group 2 had epidural steroid injections, and Group 3 was the control group. Each patient received diclofenac and participated in a home exercise program. Follow-up was at six months. All groups demonstrated significant improvements in terms of pain and function, with the group receiving epidural injections showing a significant improvement over controls at the two-week time point. The authors showed that both epidural injections and physical therapy seemed to be effective treatments in this group of patients with lumbar spinal stenosis at the time of the six-month follow-up. This was an excellent study looking at conservative treatments in a prospective manner, and we believe that it may affect what we prescribe for our patients.

Kuijper B, Tans JT, Beelen A, Nolle F, de Visser M. Cervical collar or physiotherapy versus wait and see policy for recent onset cervical radiculopathy: randomised trial. *BMJ.* 2009;339:b3883.

Two hundred and five patients with acute cervical radiculopathy were randomized to cervical collar, physical therapy, or observational treatment and were assessed at three weeks, six weeks, and six months. Treatment with either a collar or physical therapy resulted in statistically significant and clinically important benefit in comparison with no treatment at three and six weeks, but no differences were seen at six months as all patients demonstrated improvement. This well-done study demonstrates that wearing a collar or participating in active exercise programs is associated with early clinical benefit in patients with acute cervical radiculopathy.

Murrey D, Janssen M, Delamarter R, Goldstein J, Zigler J, Tay B, Darden B. Results of the prospective, randomized, controlled multicenter Food and Drug Administration Investigational Device Exemption study of the ProDisc-C total disc replacement versus anterior discectomy and fusion for the treatment of 1-level symptomatic cervical disc disease. *Spine J.* 2009;9:275-86.

This prospective, randomized, controlled clinical trial, performed in accordance with FDA guidelines, assessed the ProDisc-C cervical total disc replacement. Fusion was compared with total disc replacement. Thirteen sites

participated, and randomization was 1:1. By all measures, the ProDisc-C total disc replacement was equivalent or superior to fusion in terms of the clinical outcomes measured. This is a very good study that strongly supports that total disc replacement may be superior to anterior discectomy and fusion for one-level pathology in the cervical spine.

Okada S, Maeda T, Ohkawa Y, Harimaya K, Saiwai H, Kumamaru H, Matsumoto Y, Doi T, Ueta T, Shiba K, Iwamoto Y. Does ossification of the posterior longitudinal ligament affect the neurological outcome after traumatic cervical cord injury? *Spine (Phila Pa 1976).* 2009;34:1148-52.

The purpose of this retrospective study was to assess whether ossification of the posterior longitudinal ligament affects neurologic outcomes in patients with acute cervical spinal cord injury. One hundred and twenty-nine patients were studied for the duration of their hospital stay, and no evidence was found that ossification of the posterior longitudinal ligament had any effect on the initial neurologic status or recovery in motor function after traumatic cervical cord injury. This study suggests that the presence of asymptomatic ossification of the posterior longitudinal ligament does not substantially increase the risk of adverse outcomes following subsequent traumatic events affecting the cervical spinal cord.

Riina J, Anderson PA, Holly LT, Flint K, Davis KE, Riew KD. The effect of an anterior cervical operation for cervical radiculopathy or myelopathy on associated headaches. *J Bone Joint Surg Am.* 2009;91:1919-23.

The authors performed a post hoc analysis of randomized controlled trials comparing cervical arthroplasty with fusion to assess the frequency and severity of associated cervicogenic headache at baseline and at the time of follow-up. Headache was a major complaint in 86% of patients, with 56% of patients rating it as severe. Surgery resulted in rapid palliation, with two-thirds of patients noting sustained improvement whereas about 10% had worsening. Surprisingly, results were better in the arthroplasty group. This well-done study confirms that cervicogenic headache is a substantial problem and that patients can be counseled that improvement is likely following surgery.

Thalgott JS, Fogarty ME, Giuffre JM, Christenson SD, Epstein AK, Aprill C. A prospective, randomized, blinded, single-site study to evaluate the clinical and radiographic differences between frozen and freeze-dried allograft when used as part of a circumferential anterior lumbar interbody fusion procedure. *Spine (Phila Pa 1976).* 2009;34:1251-6.

In this prospective randomized trial, the authors compared two methods of femoral ring allograft preparation, freeze-dried and fresh-frozen, used for anterior lumbar interbody fusion. Patients were followed for twenty-four months and were assessed with regard to fusion, complications, functional outcome, and pain. Both methods of graft preparation were noted to be associated with similar pain and outcomes scores. Patients managed with freeze-dried allografts had a higher rate of pseudarthrosis, with six patients requiring revision, as compared with only one patient from the fresh-frozen cohort. This study adds to growing concerns with the use of freeze-dried allografts and supports the continued use of fresh-frozen allografts despite the increased costs and difficulties associated with storage.

Walton DM, Pretty J, MacDermid JC, Teasell RW. Risk factors for persistent problems following whiplash injury: results of a systematic review and meta-analysis. *J Orthop Sports Phys Ther.* 2009;39:334-50.

Whiplash-associated disorder is the most commonly reported injury following motor-vehicle accidents. A systematic review and meta-analysis was performed from eleven cohorts (n = 3193) to identify factors that might predict a poor prognosis. No postsecondary education, female sex, a history of previous neck pain, a baseline neck pain intensity >55 of 100, the presence of neck pain at baseline, the presence of headache at baseline, catastrophizing, a whiplash-associated disorder grade of 2 or 3, and no seat belt in use at the time of collision were the nine factors that were found to be significant predictors on the basis of the odds ratio and confidence limits.

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Wardlaw D, Cummings SR, Van Meirhaeghe J, Bastian L, Tillman JB, Ranstam J, Eastell R, Shabe P, Talmadge K, Boonen S. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. *Lancet*. 2009;373:1016-24.

This randomized controlled trial was performed at twenty-one sites in eight countries. One hundred and forty-nine patients received kyphoplasty, and 151 received nonoperative care. The study was funded by Medtronic Spine. Adverse events did not differ between the groups. The one-month SF-36 physical component score improved significantly more in the kyphoplasty group than in the nonoperative treatment group. This is a very well-done study, although funded by industry, that suggests that kyphoplasty should strongly be considered in this class of patients.

Weinstein JN, Lurie JD, Tosteson TD, Zhao W, Blood EA, Tosteson AN, Birkmeyer N, Herkowitz H, Longley M, Lenke L, Emery S, Hu SS. Surgical compared with nonoperative treatment for lumbar degenerative spondy-

lolisthesis. Four-year results in the Spine Patient Outcomes Research Trial (SPORT) randomized and observational cohorts. *J Bone Joint Surg Am*. 2009;91:1295-304.

The authors present the four-year results of the randomized and observational arms of the Spine Patient Outcomes Research Trial (SPORT) for patients with degenerative spondylolisthesis. The Oswestry Disability Index and SF-36 were used for outcomes assessments. In the randomized cohort, both operative and nonoperative treatment groups experienced high rates of crossover, with 54% of patients in the nonoperative treatment group undergoing surgery and 34% of the operative treatment group instead continuing with nonoperative care. An intent-to-treat analysis demonstrated no difference between operative and nonoperative care; however, the as-treated analysis demonstrated significantly greater improvement in the operatively managed patients as compared with the nonoperatively managed patients. This study adds to the growing data from the SPORT study and suggested continued good intermediate-term results following surgery for the treatment of degenerative lumbar spondylolisthesis.